

Application No.: PCT/EP00/04445

Applicant: Biopharm Gesellschaft zur biotechnologischen Entwicklung von
Pharmaka mbH"Neuroprotective properties of GDF-15, a novel member of the TGF- β superfamily"

Our Ref: B 1991 - py / js

Claims

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Julia > 3. The pharmaceutical composition according to claim 1 or 2, wherein the protein containing the 7 Cys-knot region of the TGF- β superfamily protects against neurodegenerative events.

4. The pharmaceutical composition according to claim 3, wherein the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs.

5. The pharmaceutical composition according to claim 4, wherein the mediators of the free radical damage are selected from the group consisting of

iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family.

5 *Q1022* 6. The pharmaceutical composition according to any one of claims 1 to 5, wherein the nucleic acid comprises at least the nucleotide sequence shown in Fig. 7A or the nucleotide sequence shown in Fig. 8A or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A or mutants thereof leading to the expression of functionally active polypeptides.

10 7. The pharmaceutical composition according to any one of claims 1 to 5, wherein the protein encoded by the nucleic acid comprises at least the primary amino acid sequence shown in Fig. 7B or the primary amino acid sequence shown in Fig. 8B or amino acid residues 14 to 111 of the sequence shown in Fig. 8B as well as homologs thereof having conservative amino acid substitutions.

15 8. The pharmaceutical composition according to any one of claims 1 to 7, wherein the mammal is a human.

20 9. The pharmaceutical composition according to any one of claims 1 to 8, wherein the neurodegenerative disorders are selected from the group of acute and/or chronic neurological and psychological disorders.

25 10. The pharmaceutical composition of claim 9, wherein the neurological and psychological disorders are caused by stroke, parkinson's disease, Alzheimer's disease or other dementias, infections of the CNS and psychiatric disorders associated with disturbances in CNS transmitter systems.

30 11. The pharmaceutical composition according to claim 10, wherein the psychiatric disorders are selected from the group consisting of depression and schizophrenia.

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12. The pharmaceutical composition according to any one of claims 1 to 11 further comprising one or more agents having neurotrophic activity or functionally active derivatives or parts thereof.

5 13. The pharmaceutical composition according to claim 12, wherein the agent is a cytokine.

10 14. The pharmaceutical composition according to claim 13, wherein the cytokine is selected from the group consisting of GDF, GDNF, TGF, activins, BMP, BDNF, NGF, EGF, CNTF and FGF.

15 15. A diagnostic kit comprising a nucleic acid containing a nucleotide sequence encoding the primary amino acid sequence of a protein containing the 7 Cys-knot region of the TGF- β superfamily or a functionally active derivative or part thereof having at least a neurotrophic effect on DAergic neurons, wherein the gene coding for the protein containing the 7 Cys-knot region of the TGF- β superfamily is transcribed and/or translated in neurons and glial cells, and/or a vector containing at least the nucleic acid and/or a protein encoded by the nucleic acid and/or an antibody or a functional fragment thereof directed against the protein, for the detection of neurodegenerative disorders in mammals.

20 16. The diagnostic kit according to claim 15, wherein the neuron and glial cells are of mammalian origin.

25 *Sv 9 A 4* 17. The diagnostic kit according to claim 15 or 16, wherein the protein containing the 7 Cys-knot region of the TGF- β superfamily protects against neurodegenerative events.

30 18. The diagnostic kit according to claim 17, wherein the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs.

19. The diagnostic kit according to claim 18, wherein the mediators of the free radical damage are selected from the group consisting of iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family.

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July 25 20. The diagnostic kit according to any one of claims 15 to 19, wherein the nucleic acid comprises at least the nucleotide sequence shown in Fig. 7A or the nucleotide sequence shown in Fig. 8A or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A or mutants thereof leading to the expression of functionally active polypeptides.

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21. The diagnostic kit according to any one of claims 15 to 20, wherein the protein encoded by the nucleic acid comprises at least the primary amino acid sequence shown in Fig. 7B or the primary amino acid sequence shown in Fig. 8B or amino acid residues 14 to 111 of the sequence shown in Fig. 8B as well as homologs thereof having conservative amino acid substitutions.

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22. The diagnostic kit according to any one of claims 19 to 21, wherein the mammal is a human.

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